STIC-ILL

From: Marx, Irene
Sent: Monday, June 14, 1999 1:46 PM
To: STIC-ILL
Subject: 09/083198

Please send to Irene Marx, Art Unit 1651; CM1, 10E05, 308-2922

Metabolic inhibitors, elicitors, and precursors as tools for probing yield limitation in taxane production by Taxus chinensis cell cultures
AU Srinivasan, V.; Ciddi, V.; ***Bringi, V.*** ; Shuler, M. L.
CS School of Chemical Engineering, Cornell University, Ithaca, NY, 14853, USA
SO Biotechnol. Prog. (1996), 12(4), 457-465

Large scale production of secondary metabolites using plant cell cultures: Opportunities, realities and challenges.
AU Venkat, K.; ***Bringi, V.*** ; Kadkade, P.; Prince, C.
CS Phyton Inc., Itacha, NY 14850 USA
SO Abstracts of Papers American Chemical Society, (1997) Vol. 213, No. 1-3, pp. AGFD 54.
Meeting Info.: 213th National Meeting of the American Chemical Society San Francisco, California, USA April 13-17, 1997

I Large scale production of secondary metabolites using plant cell cultures: Opportunities, realities and challenges
AU Venkat, K.; ***Bringi, V.*** ; Kadkade, P.; Prince, C.
CS Phyton, Inc., Ithaca, NY, 14850, USA
SO Book of Abstracts, 213th ACS National Meeting, San Francisco, April 13-17 (1997), AGFD-054 Publisher: American Chemical Society, Washington, D. C.

Production of ***taxol*** by cell culture of Taxus. For development of techniques for industrial production
AU Hara, Yasuhiro; Yukimune, Yukihito
CS Mitsui Petrochem. Ind., Ltd., Yamaguchi, 740, Japan
SO Farumashia (1996), 32(7), 806-809
CODEN: FARUAW; ISSN: 0014-8601
DT Journal; General Review
LA Japanese

TI Effect of picloram and methyl ***jasmonate*** on growth and ***taxane*** accumulation in callus culture of Taxus X media var. Hatfieldii.
AU Furmanowa, M.; Glowniak, K.; Syklowska-Baranek, K.
SO Plant cell, tissue and organ culture, 1997. Vol. 49, No. 1. p. 75-79
Publisher: Dordrecht, The Netherlands : Kluwer Academic Publishers.

TI Large-scale plant cell culture
AU Roberts, Susan C.; Shuler, Michael L.
CS Sch. Chemical Eng., Cornell Univ., Ithaca, NY, 14853-5201, USA
SO Curr. Opin. Biotechnol. (1997), 8(2), 154-159

STIC-ILL

From: Marx, Irene
Sent: Monday, June 14, 1999 1:46 PM
To: STIC-ILL
Subject: 09/083198

Please send to Irene Marx, Art Unit 1651; CM1, 10E05, 308-2922

Metabolic inhibitors, elicitors, and precursors as tools for probing yield limitation in taxane production by Taxus chinensis cell cultures
AU Srinivasan, V.; Ciddi, V.; ***Bringi, V.*** ; Shuler, M. L.
CS School of Chemical Engineering, Cornell University, Ithaca, NY, 14853, USA
SO Biotechnol. Prog. (1996), 12(4), 457-465

Large scale production of secondary metabolites using plant cell cultures: Opportunities, realities and challenges.
AU Venkat, K.; ***Bringi, V.*** ; Kadkade, P.; Prince, C.
CS Phyton Inc., Itacha, NY 14850 USA
SO Abstracts of Papers American Chemical Society, (1997) Vol. 213, No. 1-3, pp. AGFD 54.
Meeting Info.: 213th National Meeting of the American Chemical Society San Francisco, California, USA April 13-17, 1997

I Large scale production of secondary metabolites using plant cell cultures: Opportunities, realities and challenges
AU Venkat, K.; ***Bringi, V.*** ; Kadkade, P.; Prince, C.
CS Phyton, Inc., Ithaca, NY, 14850, USA
SO Book of Abstracts, 213th ACS National Meeting, San Francisco, April 13-17 (1997), AGFD-054 Publisher: American Chemical Society, Washington, D. C.

Production of ***taxol*** by cell culture of Taxus. For development of techniques for industrial production
AU Hara, Yasuhiro; Yukimune, Yukihito
CS Mitsui Petrochem. Ind., Ltd., Yamaguchi, 740, Japan
SO Farumashia (1996), 32(7), 806-809
CODEN: FARUAW; ISSN: 0014-8601
DT Journal; General Review
LA Japanese

TI Effect of picloram and methyl ***jasmonate*** on growth and ***taxane*** accumulation in callus culture of Taxus X media var. Hatfieldii.
AU Furmanowa, M.; Glowniak, K.; Syklowska-Baranek, K.
SO Plant cell, tissue and organ culture, 1997. Vol. 49, No. 1. p. 75-79
Publisher: Dordrecht, The Netherlands : Kluwer Academic Publishers.

TI Large-scale plant cell culture
AU Roberts, Susan C.; Shuler, Michael L.
CS Sch. Chemical Eng., Cornell Univ., Ithaca, NY, 14853-5201, USA
SO Curr. Opin. Biotechnol. (1997), 8(2), 154-159

is metal toxicities. Evidence has emerged that non-
ay significantly alter the overall oxidative status of
. due to a given oxidant is inversely related to the
:o stress by generating oxidant signals to mobilize a
ivity of those enzymes have an effect on cellular
ınd retained in wine have been found in vitro, to
late nitric oxidation production and promote vaso-
ıportant to foods, plants and humans. Nutrients that
as valuable not only in combating the deteriorative
gnaling that is an integral part of the response.

ATECHIN IN RATS. M. K. Piskula, J. Terao,
i 305, Japan

the defence system of organism against oxidative
ving positive influence of dietary flavonoids on
ng antioxidtive activity of flavonoids in different
ts after ingestion and absorption. Looking for an
f (-)epicatechin (EC), a commonly consumed
ısma level of metabolites was measured. 1h after
C- glucuronide (11μM), EC-glucuronide-sulfate
hile the concentration of the first two started to
3 hours, the third one had its maximum 1h later
ab. 50% of all EC metabolites.Studies on the site
:sted EC is glucuronidation, occurring already on
portal vein exclusively in a conjugated form and

HAMSTER MODEL. Dietrich Rein[1], Wallace H.
ood Sci. & Tech. University of California, Davis,
Albany, CA 94710

ınd seed oils moderate the development of
sent in these foods. The aim of this study was to
o test the effects of food components on the
lipid deposition was investigated in hamsters fed
irement of 3 IU or 30 IU vitamin E. After 30
en groups, and the high density lipoprotein
; atherogenic. Atherosclerosis was measured by
ı new photomicroscopy scanning technique. The
than in the 3 IU vitamin E group ($p < 0.03$). This
n-6 and n-3 fatty acids together with cholesterol
to vitamin E with respect to the development of
: effects of individual food components *in vivo*.

TIVITIES OF α-TOCOPHEROL AND ITS
:rao[2], [1]Noda Institute for Scientific Research,
ch Institute, Tsukuba, Ibaraki 305, Japan.

ıt and to suppress the oxidative hemolysis of
yl derivative of α-tocopherol (phosphatidyl-
α-tocopherol, PCh, and 2,2,5,7,8-
ıan erythrocytes, it was found that the antihemolytic activity was significantly enhanced by introducing phospholipid moiety into chromanol. PCh was incorporated into erythrocyte membrane and acted as an effective protector against oxidative hemolysis and membrane lipid peroxidation. The erythrocyte into which PCh was incorporated also has an inhibitory effect against the accumulation of cholesterol ester hydroperoxides in plasma. The relationship between structure of α-tocopherol derivatives and their antioxidant and antihemolitic activities will be discussed.

052. **INTERACTIONS OF TOCOPHEROL AND FATTY ACIDS WITH MODEL PHOSPHOLIPID MEMBRANES: IMPLICATIONS FOR ANTIOXIDANT ACTIVITY OF VITAMIN E.** D.F. Church, * T.R. Dugas, # J.D. Blazier, # G.M. Pineda. # *Radical Technologies, Baton Rouge,LA 70810 and #Department of Chemistry, Louisiana State University, Baton Rouge, LA 70803.

Kinetic studies show that α-tocopherol inhibits lipid peroxidation in unilamellar liposomes too slowly to act as an effective antioxidant at physiologically relevant concentrations. Antioxidant effectiveness is restored when free oleic acid is also incorporated into the model system. ESR spin-label measurements of the inclusion volumes of liposomes with added tocopherol and/or oleic acid suggest that neither of these, alone or together, substantially affect liposome structure. Both spin-label and differential scanning calorimetry studies show that tocopherol significantly increases membrane order and decreases fluidity, while the inclusion of oleic acid reverses these changes. Thus, physico-chemical interactions between tocopherol, free fatty acids and membrane phospholipds appear to control the inhibition of lipid peroxidation in membranes by tocopherol.

053. ANTIOXIDANT EVALUATION OF PHYTOCHEMICALS IN BIOLOGICAL SYSTEMS. E.N. Frankel, Department of Food Science & Technology, University of California, Davis, California 95616

The true impact of biological oxidation is very controversial because of the questionable methodology used to measure lipid oxidation. Several non-specific assays have been introduced recently to test the "antioxidant capacity" of biological tissues and fluids, using artificial radicals as probes. These non-specific methods do not provide any information on what lipid or protein target is protected and may be confounded by many factors in complex biological systems including effects that may not be derived from lipid oxidation. To learn about the real effects of antioxidants, it is important to obtain specific chemical information about what products of lipid oxidation are inhibited. Several specific assays are needed to elucidate how lipid oxidation products act in the complex multi-step mechanism of lipid oxidative deterioration and damage in biological tissues. The methodology to evaluate natural antioxidants must be carefully interpreted depending on the system and the method used to determine lipid oxidation.

054. LARGE SCALE PRODUCTION OF SECONDARY METABOLITES USING PLANT CELL CULTURES: OPPORTUNITIES, REALITIES AND CHALLENGES
K. Venkat, V. Bringi, P. Kadkade, and C. Prince, Phyton, Inc., Ithaca, NY 14850

The plant kingdom has historically been a major source of valuable medicinal compounds and healing agents. Unfortunately these compounds often occur in low yields in nature; further they require complex isolation and purification procedures. Plant cell culture technology offers a potential means to address these problems. Although elements of this technology have been around for many years, its widespread commercial use have not been possible due to a number of factors. Recent developments have brought this technology much closer to commercial application to large scale manufacturing of therapeutic and other valuable products.

Phyton has invested more than 150 man-years of effort to address the commercial issues of plant cell culture technology. Under a long-term collaborative relationship with Bristol-Myers Squibb (BMS) Company, Phyton is engaged in the development and commercialization of a plant cell culture process for the production of paclitaxel (the active ingredient of Taxol®; Taxol is the registered trademark of BMS). Through its wholly-owned subsidiary, Phyton Gesellschaft für Biotechnik mbH, Phyton operates the world's largest dedicated plant cell culture facility in Ahrensburg, Germany. It has a bioreactor capacity of up to 75,000 liters in size.

Several key issues relating to the development and practice of commercial plant cell culture processes for Taxol® and other high value compounds will be discussed.